

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
13 October 2005 (13.10.2005)

PCT

(10) International Publication Number
WO 2005/095449 A1

(51) International Patent Classification⁷: **C07K 14/475**,
1/14, 1/20

(21) International Application Number:
PCT/EP2005/002177

(22) International Filing Date: 2 March 2005 (02.03.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
04004950.4 3 March 2004 (03.03.2004) EP

(71) Applicant (*for all designated States except US*): **F. HOFF-
MANN-LA ROCHE AG** [CH/CH]; Grenzacherstrasse
124, CH-4070 Basel (CH).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **HESSE, Friederike**
[DE/DE]; Ganghoferstrasse 23, 80339 München (DE).
LANZENDOERFER, Martin [DE/DE]; Waldeslust 4,
81377 Muenchen (DE). **PAPADIMITRIOU, Apollon**
[DE/DE]; Bachstrasse 38a, 83673 Bichl (DE). **STRACKE,**
Jan [DE/DE]; Seeshaupter Strasse 18b, 82377 Penzberg
(DE).

(74) Agent: **SCHREINER, Siegfried**; Roche Diagnostics
GmbH, Patent Department (TR-E), Postfach 11 52, 82372
Penzberg (DE).

(81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

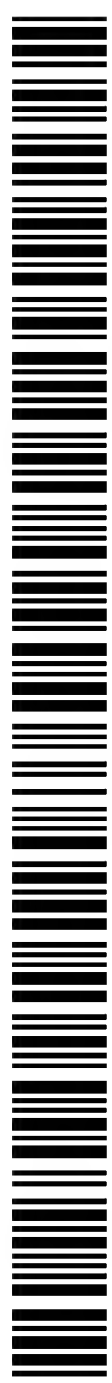
Published:

— *with international search report*
— *before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: METHOD FOR THE PURIFICATION OF AN N-TERMINAL FRAGMENT OF HEPATOCYTE GROWTH FACTOR

(57) Abstract: A method for the production of the N-terminal four kringle-containing fragment of hepatocyte growth factor (NK4) by expression of a nucleic acid encoding said NK4 in a microbial host cell, isolation of inclusion bodies containing said NK4 in denatured form, solubilization of the inclusion bodies and naturation of the denatured NK4, characterized in that solubilization and naturation are performed at pH 7-9 in phosphate buffered solution, provides NK4 in high purity and high yield.



WO 2005/095449 A1